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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/538,736	08/11/2005	Mara Brancaccio	4636-25	7505

23117 7590 05/03/2006

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EXAMINER	
GEMENIANO, MALOU C	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 05/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/538,736	BRANCACCIO ET AL.	
	Examiner	Art Unit	
	Malou C. Gemeniano	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 August 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *6/14/05* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/14/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

In response to the election restriction filed on 3/10/06, applicant elected with traverse Group1 (claims 1-17 and 20-22) drawn to non-human transgenic animals and cells therefrom, which have altered expression, for examination on the merits. The traversal based on the argument that Group 4 (claims 24-25) and Group 2 (18 and 23) should be examined because they are the first recitation of a process of manufacture and the first recitation of the first process of use is persuasive and will be included for examination on the merits. However, the traversal based on the argument that there is a single general inventive concept or technical feature that links non-human transgenic animal with an altered melusin expression with claims 26-29 is not persuasive. In fact, the animal of group 1 is a non-human transgenic animal characterized with altered melusin expression due to an inactivation of melusin wherein the inactivation is performed by genetic approaches such as homologous recombination. However, the non-human animal of Group 5-8 (claims 26-29) is not a transgenic animal nor is melusin expression altered by genetic approaches but rather by natural or synthetic compounds as explicitly recited in claim 26. As such, Group 5-8 lack the same technical feature as Group 1 and will not be included in the examination. The following Office action is an examination on the merits of claims 1-25.

Specification

The incorporation of essential material in the specification by reference to an unpublished U.S. application, foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference, if the material is relied upon to overcome any objection, rejection, or other requirement imposed by the Office. The amendment must be accompanied by a statement executed by the applicant, or a practitioner representing the applicant, stating that the material being inserted is the material previously incorporated by reference and that the amendment contains no new matter. 37 CFR 1.57(f).

Claim Rejections - 35 USC § 112-1st

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim Rejections - 35 USC § 112 – written description

Claims 1-25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to any person skilled in the art to which it pertains, or with which it is most nearly connected, at the time the application was filed, that the inventor, at the time the application was filed, had possession of the claimed invention.

Claim 1-25 when given the broadest reasonable interpretation encompasses large genus of non-human transgenic animals and cells having a large genus of altered melusin expression wherein inactivation and/or altered expression is performed by any genetic approach wherein hypertensive condition is generated by any surgical approach, any pharmacological treatment of hypertensive drug and/or unspecified high sodium diet such that said non-human transgenic animal develops heart dilation, heart hypertrophy and heart failure due to altered melusin expression. For example the claims encompasses any melusin gene wherein the altered expression (included decrease as well as increase expression) causes development of heart hypertrophy, heart dilation and/ or heart failure. The specification fails to describe what DNA molecule falls into this large genus as the as core structure and characteristics of such animals encompasses by these broad claims.

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail such that the Artisan can reasonably conclude that the inventor(s) had possession of the claimed invention. Such possession may be demonstrated by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and/or formulae that fully set forth the claimed invention. Possession may be shown by an actual reduction to practice, showing that the invention was "ready for patenting", or by describing

distinguishing identifying characteristics sufficient to show that Applicant was in possession of the claimed invention (January 5, 2001 Fed. Reg., Vol. 66, No. 4, pp. 1099-11). Moreover, MPEP 2163 states:

> [A] biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence.

Overall, what these statements indicate is that the Applicant must provide adequate description of such core structure and function related to that core structure such that the Artisan could determine the desired effect. Hence, the analysis below demonstrates that Applicant has not determined the core structure for full scope of the claimed genera.

In analyzing whether the written description requirement is met for genus claims, it is first determined whether a representative number of species have been described by their complete structure. When given the broadest reasonable interpretation, "altered melusin gene expression" recited in claim 1 encompasses any melusin gene or variant or mutation that causes an altered expression of melusin such that said non-human transgenic animal develops heart hypertrophy, heart dilation, heart failure. In the instant case, Applicant provides only one example of the genus "altered expression of melusin". There is a large genus of mutations and variants encompassed by "altered expression of melusin". In addition, the specification does not provide sufficient description regarding core structure and characteristics of all possible cells types that lack melusin expression. As such, there are cell types that naturally do not express melusin since melusin is restricted to striated muscles (Brancaccio et al. The Journal of Biological Chemistry 1999 Vol. 274 pp29282-29268). For example, description of all cells that naturally do not have melusin expression is lacking. Moreover, the specification does not provide any disclosure as to what would have been the required structure for all these variants. As

applicant failed to sufficiently describe in the specification any disclosure as to what would have been the required structure.

Applicant's attention is directed to *In re Shokal*, 113 USPQ 283 (CCPA 1957), wherein it is stated:

> It appears to be well settled that a single species can rarely, if ever, afford sufficient support for a generic claim. *In re Soll*, 25 CCPA (Patents) 1309, 97 F2d 623, 38 USPQ 189; *In re Wahlforss*, 28 CCPA (Patents) 867, 117 F2d 270, 48 USPQ 397. The decisions do not however fix any definite number of species which will establish completion of a generic invention and it seems evident therefrom that such number will vary, depending on the circumstances of particular cases. Thus, in the case of small genus such as the halogens, consisting of four species, a reduction to practice of three, perhaps even two, might serve to complete the generic invention, while in the case of a genus comprising hundreds of species, a considerably larger number of reductions to practice would probably be necessary.

In conclusion, this limited information is not deemed sufficient to reasonably convey to one skilled in the art that Applicant is in possession of all non-human transgenic animal and/or cell having all the possible altered variations of melusin expression wherein animal develops heart hypertrophy, heart dilation and heart failure. Thus it is concluded that the written description requirement is not satisfied for the large broad claimed genus.

Claim Rejections - 35 USC § 112-enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for

A transgenic melusin knockout mice wherein the endogenous melusin is disrupted wherein the said transgenic mice exhibits normal cardiac structure and function in physiological conditions wherein when said transgenic mouse is subjected to pressure overload wherein pressure load is a condition that induces a hypertrophic responses in wildtype controls, melusin knockout mice exhibit abnormal cardiac remodeling, dilated cardiomyopathy and contractile dysfunction;

does not reasonably provide enablement for any non-human transgenic animal having altered melusin expression wherein inactivation and/or altered expression is performed by any genetic approach wherein hypertensive condition is generated by any surgical approach, any pharmacological treatment of hypertensive drug and/or unspecified high sodium diet such that said non-human transgenic animal develops heart dilation, heart hypertrophy and heart failure due to altered melusin expression;

does not reasonably provide enablement for screening compounds that is pharmacologically active in the prevention and/or treatment of heart failure comprising any administration route of unspecified compounds to the non-human transgenic animal and/or cell having altered expression of melusin;

does not reasonably provide enablement for studying a heart failure, congestive heart failure, dilated cardiomyopathy, hypertensive cardiomyopathy, hypertrophic cardiomyopathy and heart infract in the non-human transgenic animal having altered expression of melusin;

does not reasonably provide enablement for preparing a any non-human transgenic animal with altered melusin gene expression comprising of steps of (i) preparing a non-human transgenic parent animal carrying an inactivated melusin allele (ii) breeding the parent transgenic animal with any non-transgenic animal; (iii) selecting transgenic animals heterozygote for melusin gene mutation (iv) breeding the heterozygote transgenic animals to select homozygote transgenic animals for the melusin gene mutation.

The claim(s) contain subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification does not enable any person skilled in the art to which it pertains or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention and breadth of claims

Claims 1-25 are drawn to a non-human transgenic animal having altered melusin expression wherein inactivation and/or altered expression is performed by any genetic approach wherein hypertensive condition is generated by any surgical approach, any pharmacological treatment of hypertensive drug and/or unspecified high sodium diet such that said non-human transgenic animal develops heart dilation, heart hypertrophy and heart failure due to altered melusin expression; methods of screening compounds using said non-human transgenic animal that is pharmacologically active in the prevention and/or treatment of heart failure; the method of studying any heart pathology using said non-human transgenic animal and methods of making a large genus of non-human transgenic animal having altered expression of melusin.

The aspects considered broad are: the breadth of a large genus of non-human transgenic animal having any altered expression of melusin, wherein inactivation and/or altered expression is performed by any genetic approach wherein any hypertensive condition is generated by any surgical approach, any pharmacological treatment or

hypertensive drug and/or unspecified high sodium diet such that said non-human transgenic animal develops heart dilation, heart hyperptrophy and heart failure due to altered melusin expression and the use of this large genus of non-human transgenic animal for screening compounds to prevent and /or treatment heart failure and studying a large genus of pathologies encompasses by heart failure. As will be shown below, these broad aspects are not enabled for their full scope embraced. The detail of the disclosure provided by the Applicant, in view of the prior Art, must encompass a wide area of knowledge to enable one of ordinary skill in the art at the time of the invention to practice the invention without undue experimentation. However, as it will be discussed below this undue experimentation has not been overcome by the as-filed application. And, due to such lack of enablement, some claims are not enabled whatsoever.

State of the prior art

Claims 1-25 are drawn to a non-human transgenic animal having altered melusin expression wherein inactivation and/or altered expression is performed by any genetic approach wherein hypertensive condition is generated by any surgical approach, any pharmacological treatment of hypertensive drug and/or unspecified high sodium diet such that said non-human transgenic animal develops heart dilation, heart hypertrophy and heart failure due to altered melusin expression; and methods of screening compounds using said non-human transgenic animal that is pharmacologically active in the prevention and/or treatment of heart failure and the methods of studying any heart pathology using said non-human transgenic animal; and methods of making a large genus of non-human transgenic animal having altered expression of melusin.

The state of the prior art, at time of invention was filed, regarding melusin and its probable functional role in cells of cardiac lineage is exemplified in the following cited references: Brancaccio et al (The Journal of Biological Chemistry 1999 Vol. 274 pp29282-29268), Shai S-Y et al. (Circulation Research 2002; 90: 458-464), and Fassler R et al (Journal of Cell Science 1996 109,2989-2999). Melusin has been isolated and partial characterized just recently wherein is had been described to interact with the β1 integrin cytoplasmic protein and expression is restricted to striated muscle tissues (Brancaccio M et al 1999 p. 29284 column 1 4th ¶ and p. 29285 Figure 2). Applicant submits that

melusin is likely to represent a new intracellular transducer of β1 integrin function in muscle cells (specification p. 2 line 31) since it binds to well known β1 integrin which is also expressed in striated cardiac and skeletal muscles (specification p. 4 line 1-4) and Fassler et al demonstrated that β1 integrin is important for normal cardiogenesis by the use of β1 integrin deficient embryonic stem cells (p. 2992, Figure 2) and β1 integrin knock-out mice (p. 2997, Figure 7). Lastly, in corroboration of the importance of β1 integrin and the protein, melusin that binds it, Shai et al demonstrated that specific excision of β1 integrin gene results in fibrosis and cardiac failure (p. 462, Figure 2).

However, since the claims encompass a large genus of non-human transgenic animal having any altered melusin expression wherein inactivation and/or altered expression is performed by any genetic approach wherein hypertensive condition is generated by any surgical approach, any pharmacological treatment of hypertensive drug and/or unspecified high sodium diet such that said non-human transgenic animal develops heart dilation, heart hypertrophy and heart failure due to altered melusin expression is considered unpredictable.

Regarding the claimed invention drawn to any non-human transgenic animal having any altered melusin expression wherein non-human transgenic animal develops heart dilation, heart hypertrophy and heart failure due to altered melusin expression is considered unpredictable since the art teaches that a disruption of endogenous melusin causes heart dilation, heart hypertrophy and heart failure upon pressure overload. Therefore, a non-human transgenic mice with an altered melusin expression wherein the melusin is over-expressed or other alterations wherein melusin is not completely knockout is not recorded in the art to have altered the phenotypes of the claimed invention. Furthermore, non-human transgenic animals wherein the alteration of melusin is an over expression of the protein would not have the phenotypes of the claimed invention. For example, De acetis et al (Circulation Research 2005 96(10):1087-1094) demonstrated the contrary by over expressing melusin which protected from cardiomyopathy due to long standing pressure overload.

Regarding the claimed invention drawn to non-human transgenic animals with an altered melusin expression wherein the melusin expression is performed by any genetic

approach would be considered unpredictable. The claims would encompass a large genus of genetic approaches such as interference RNA or DNA, antisense technology, nuclear transfer, over expression of transdominant negative proteins. However, to make a non-human transgenic animal using such genetic approach such the said animal would have the phenotypes of embraced by the claims would be considered unpredictable. Houdebine L-M (Journal of Biotechnology 98 (2002) 145-160) teaches that common problems with antisense RNA technology is that antisense RNA and the targeted mRNA sequences have little chance to interact. Both partners have often secondary structure and they are associated with proteins rendering their contact unlikely (p. 152, 1st column 2nd ¶). In corroboration Hughes et al (Drug discovery today 2001 no. 6 p.303-315) teaches that common problems with antisense oligonucleotides the majority of internalized antisense oligonucleotides is sequestered into endosome or lysosomal compartments therefore causing trafficking problems to the point where most antisense oligonucleotides would not exert its effects (p. 304 2nd column 2nd ¶). In light of the cited references, it would not be predictable to make any non-human transgenic animal with an altered melusin expression using any genetic approaches especially antisense RNA/DNA and DNA/RNA interference such that the said non-human transgenic animal would exhibit the claimed phenotypes as embraced by the claims.

The totality of the cited references is reflected of the state of the art regarding the unpredictability of the phenotypes of a non-human transgenic mouse a non-human transgenic animal having altered melusin expression wherein inactivation and/or altered expression is performed by any genetic approach and/or stable or transient modification of melusin expression wherein hypertensive condition is generated by any surgical approach, any pharmacological treatment of hypertensive drug and/or unspecified high sodium diet such that said non-human transgenic animal develops heart dilation, heart hypertrophy and heart failure due to altered melusin expression. At the time of filing, the resulting phenotype(s) of a non-human transgenic animal commensurate of the claims is considered unpredictable. In addition, the method of selecting a compound that is pharmacologically active in the prevention and/or treatment of heart failure would be unpredictable in view of the unpredictability of the phenotype of the non-human

transgenic animal commesurate of the claims. Lastly, the method of studying heart pathology using the non-human transgenic animal would not be predictable for reasons state above.

The predictability or lack thereof in the art

The predictability or lack thereof in the art refers to the ability of one skilled in the art to extrapolate the disclosed or known results to the claimed invention. If one skilled in the art can readily anticipate the effect of a change within the subject matter to which the claimed invention pertains, then there is predictability in the art. On the other hand, if one skilled in the art cannot readily anticipate the effect of a change within the subject matter to which that claimed invention pertains, then there is lack of predictability in the art.

Guidance in the Specification and working example

Analysis of Quantity of Experimentation

The applicant claims broadly any non-human animal having any altered expression of melusin wherein the alteration in expression is performed by any genetic approach and/or stable or transient modification of melusin expression wherein hypertensive condition is generated by any surgical approach, any pharmacological treatment of hypertensive drug and/or unspecified high sodium diet such that said non-human transgenic animal develops heart dilation, heart hypertrophy and heart failure due to altered melusin expression; and methods of screening compounds using said non-human transgenic animal that is pharmacologically active in the prevention and/or treatment of heart failure and the methods of studying any heart pathology using said non-human transgenic animal; and methods of making a large genus of non-human transgenic animal having altered expression of melusin.

First, in regards to the non-human transgenic animal having any altered expression of melusin, the specification does not describe in sufficient detail and/or provide detail as to obtain any organism other than specifically the melusin knockout mice exhibiting normal cardiac structure and function in physiological conditions wherein when said transgenic mouse is subjected to pressure overload wherein pressure load is a condition that induces a hypertrophic responses in wildtype controls, melusin

knockout mice exhibit abnormal cardiac remodeling, dilated cardiomyopathy and contractile dysfunction.

In view of the unpredictability of the prior art, one ordinary skilled in the art would perform undue experimentation to make a large genus of animals having any altered expression of melusin wherein the said animal is characterized by the phenoytpes commensurate of the claims. As such, there is need for specific detail of methods to make and use a large genus animals with phenotypes commensurate of the claims.

In regards to the non-human transgenic animal having any altered expression of melusin, wherein the said altered melusin expression is performed by stable or transient modification of the melusin expression at transcriptional, translational or post-translational level and/or performed by any genetic approach such as antisense RNA or DNA and RNA or DNA interference. The specification offers no guidance or examples as to perform any transient modification. Moreover, the applicant is silent as to the steps and core structure of the antisense RNA used to perform such alteration in melusin gene expression. The specification offers no other description, guidance and working example except for the production of a melusin-null transgenic mice using cassette containing IRES sequences linked to the LacZ gene followed by the neomycin resistance gene (Example 1). One ordinary skilled in the art was to obtain a non-human animal of the claimed invention, one ordinary skilled would not know if they were in possession of the invention as the Applicant provided no description in the specification of the core structure or characteristic of the non-human animal and one ordinary skilled in the art would not know how to use such an animal in regards to its application towards neurodegenerative diseases. Therefore, one ordinary skilled in the art would have the burden to perform undue experimentation to make and use the invention.

In regards to the claimed invention drawn to non-human animal having any altered expression of melusin wherein the said animal develops impaired hypertrophy, heart dilation and heart failure. These claims encompass an animal with any alteration in melusin expression that develops these phenotypes without requirement of animal subjected to pressure overload. The claims are not enabled for such an animal since the specification offers no example of such an animal nor guidance to obtain such an animal.

The specification offers description of only the following: A melusin knockout mice exhibiting normal cardiac structure and function in physiological conditions wherein when said transgenic mouse is subjected to pressure overload wherein pressure load is a condition that induces a hypertrophic responses in wildtype controls, melusin knockout mice exhibit abnormal cardiac remodeling, dilated cardiomyopathy and contractile dysfunction.

In regard to the claimed invention drawn to non-human transgenic animal having any altered expression of melusin wherein the said animal develops hypertensive condition generated by any surgical operation, any hypertensive drugs and/or high sodium diet. The claims are not enabled for such an animal since specification offer no example of such animal nor guidance to obtain a non-transgenic animal characterized with the phenotypes commensurate of the claims. For example, the specification offers guidance for a specific surgical procedure to impose cardiac pressure only (Example 2 p. 14 lines 20-35). However, the Applicant submits that these phenotypes are not exhibited when using hypertensive drugs (Example 3); therefore, supporting the argument that a non-human transgenic having any altered expression of melusin wherein the said animal develops hypertensive conditions using any hypertensive drugs or subjected to any high sodium diet that would induce the phenotypes of the non-human transgenic animal commensurate of claims.

In regards to the claimed invention drawn to the methods of selecting compounds that is pharmacologically active in the prevention and/or treatment of heart failure, the specification is silent as to the steps and procedure of the screening method as well as offer no guidance of administration such compounds. In regards to the claimed invention drawn to the method of studying heart pathology wherein the heart pathology is selected from the group consisting of: heart failure, congestive heart failure, dilated cardiomypathy, hypertensive cardiomyopathy, hypertrophic cardiomyopathy and heart infarct. The specification offers no description of such pathologies and how they are different from each other. Without guidance, steps and procedure to offer to study these pathologies one ordinary skilled in the art is left with undue experimentation to use the invention commensurate of the claims.

The specification lacks sufficient detail, working examples and guidance such as to provide to one skilled in the art to make and use the invention commensurate of the claims.

In view of the unpredictability of the Art, it is essential to provide sufficient description and/or guidance in the specification to provide one ordinary skilled in the art to make and use invention commensurate of the broadness of the claims. However, Applicant provides no detail of this. Therefore one skilled in the art would have to perform undue experiment to make and use the claimed invention. Therefore, Applicant provides insufficient guidance and/or working example for a skilled artisan to reasonably enable the claimed invention of non-human transgenic animal having altered melusin expression wherein inactivation and/or altered expression is performed by any genetic approach wherein hypertensive condition is generated by any surgical approach, any pharmacological treatment of hypertensive drug and/or unspecified high sodium diet such that said non-human transgenic animal develops heart dilation, heart hypertrophy and heart failure due to altered melusin expression; and methods of screening compounds using said non-human transgenic animal that is pharmacologically active in the prevention and/or treatment of heart failure and the methods of studying any heart pathology using said non-human transgenic animal; and methods of making a large genus of non-human transgenic animal having altered expression of melusin.

Due to the large quantity of experimentation necessary to generate and use the infinite number of derivatives of transgenic animals commensurate of the claims, one skilled in the Art will have to perform extensive experimentation with each of these parameters to find the embodiments embraced by the claims, and as such, this experimentation would be considered undue.

Claim Rejections - 35 USC § 101 and Claim Rejections - 35 USC § 112

Claims 18, 19 and 23 provide for the use of an animal, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 18, 19 and 23 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

In conclusion, claims 1-25 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Malou C. Gemeniano whose telephone number is 571-272-6451. The examiner can normally be reached on 8am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications regarding the formalities should be directed to Patent Analyst Dianiece Jacobs, whose telephone number is (571)-272-0532.

For all other customer support, please call the USPTO Call Center (UCC) at (800)-786-9199.

Malou C. Gemeniano, Ph.D
Examiner, USPTO, AU 1632

DAVE TRONG NGUYEN
SUPERVISORY PATENT EXAMINER